Paper No. 22

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte STALEY A. BROD

Appeal No. 1999-2502
Application No. 08/631,470

ON BRIEF

Before WINTERS, WILLIAM F. SMITH, and GREEN, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-20. This appeal is related to Appeal Nos. 1999-2508 (Application No. 08/844,731) and 2000-1094 (Application No. 08/946,710).

Claims 1, 8, 13, and 19 are representative of the subject matter on appeal, and read as follows:

1. A method of treating an auto-immune disease in an animal comprising the step of orally administering a type one interferon to said animal such that the type one interferon is ingested immediately upon oral administration.

8. A method of decreasing the severity or frequency of a relapse of multiple sclerosis in a human comprising the step of orally administering a type one interferon to said animal such that the type one interferon is ingested immediately upon oral administration.

13. A method of reducing inflammation associated with an auto immunedisease in an animal comprising the step of orally administering a type one interferon to said animal such that the type one interferon is ingested after oral administration.

19. A method of decreasing the levels of a cytokine in an individual having multiple sclerosis, comprising the step of orally administering a type one interferon to said individual, wherein said cytokine is selected from the group consisting of TGF-β, IL-2, IL-10, IFN-γ and ICAM-1; and wherein said type one interferon is ingested immediately upon oral administration.

The examiner relies upon the following references:

Cummins, Jr. (Cummins) 5,019,382 May. 28, 1991

Shibutani et al. (Shibutani) "Toxicity Studies of Human Fibroblast Interferon Beta (I) Acute and Subacute Toxicity Studies in Mice and Rats," Iyakuhin Kenkyu , Vol. 18 (4), pp. 571-582 (1987)

Claims 1-12 and 19-20 stand rejected under 35 U.S.C. § 112, first paragraph, for containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that applicant had possession of the claimed invention at the time of filing. Claims 1-4, 6-11, and 13-20 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Cummins, claims 5 and 12 stand rejected under 35 U.S.C. § 103(a) as obvious over the teachings of Cummins, and claims 1-20 stand rejected under 35 U.S.C. § 103(a) as being rendered obvious by the combination

of Cummins and Shibutani. After careful review of the record and consideration of the issues before us, we affirm the rejection under 35 U.S.C. § 112, first paragraph, the rejection under 35 U.S.C. § 102(b) as it pertains to claims 1-3, 6-11, 13-15, and 17-19, and the rejection under 35 U.S.C. § 103(a) over Cummins of claims 5 and 12, but reverse the rejection under 35 U.S.C. § 102(b) as it pertains to claims 4, 16, and 20, and the rejection under 35 U.S.C. § 103(a) of claims 1-20 over the combination of Cummins and Shibutani.

BACKGROUND

The invention of the instant application is drawn to the treatment of auto-immune diseases in an animal, including humans, by orally administering a type one interferon to the animal. The interferon may be alpha or beta interferon, and is preferably human recombinant interferon, rat interferon, or murine interferon. See Specification, page 16.

According to the specification, the type one interferon is administered at a dosage that would effectively inhibit the onset or reoccurrence of an autoimmune disease. In addition, a wide variety of auto-immune diseases may be treated according to the invention, "includ[ing] multiple sclerosis, rheumatoid arthritis, diabetes mellitus, psoriasis, organ-specific auto-immune diseases, chronic inflammatory demyelinating polyradiculoneuropathy and Guillain-Barré syndrome." Id. at 17.

DISCUSSION

The panel would like to initially note that review of the issues on appeal was severely hampered by the lack of claim-by-claim analysis by the examiner, i.e., the use of "shotgun" rejections.

Findings of fact and the conclusions of law must be made in accordance with the Administrative Procedure Act, 5 U.S.C.§ 706 (A), (E) (1994). See Zurko v. Dickinson, 527 U.S. 150, 158, 119 S.Ct. 1816, 1821, 50 USPQ2d 1930, 1934 (1999). Findings of fact relied upon in making the rejections are reviewed by the Court of Appeals for the Federal Circuit, or reviewing court, for substantial evidence within the record. See In re Gartside, 203 F.3d 1305, 1315, 53 USPQ2d 1769, 1775 (Fed. Cir. 2000). A determination of whether the findings of fact are supported by the record is difficult to make, however, if the examiner does not explicitly set forth those findings.

1. Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-12, 19 and 20 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to the skilled artisan that the inventor had possession of the claimed subject matter at the time of filing. Specifically, the examiner contends that there is no support that the interferon is ingested "immediately upon" oral administration. See Examiner's Answer, page 6.

Appellant asserts that the phrase "ingested immediately upon oral administration" is supported by the description of the animal experiments in the instant specification, wherein interferon was "administered directly to the distal esophagus, stomach and small intestine via a 20 gauge ball point needle." Appeal Brief, page 21.

Appellant appears to be arguing that the meaning of the limitation "ingest immediately" is that the interferon has little contact with the oral and/or pharyngeal mucosa, but rather is adsorbed by the distal esophagus, stomach and small and intestine. The specification, however, does not support such a

limited definition for ingest. Ingest, as used in common usage, means "[t]o take or absorb (food) into the body." The American Heritage College Dictionary, Fourth Ed. Houghton Mifflin Co. (2002). See, e.g., Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1584 n.6, 39 USPQ2d 1573, 1578 n.3 (Fed. Cir. 1996) (noting that dictionary definitions may be relied upon in construing claim limitations "so long as the dictionary definition does not contradict any definition found in or ascertained by a reading of the patent documents"). The common usage of the term "ingest" does not exclude the adsorption by the oral and/or pharyngeal mucosa, and in fact, because the specification states that the α-interferon is to be administered orally, the skilled artisan, when reading the specification, would expect such adsorption.

Moreover, the examples relied upon by appellant as supporting the more limited definition of ingest does not contradict this finding, as the skilled artisan, would not interpret administration of interferon directly to the distal esophagus, stomach and small intestine via a 20 gauge ball point needle as oral administration. Thus, the skilled artisan would not immediately understand that "ingest" requires limiting contact with the oral and/or pharyngeal mucosa, and the rejection under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to the skilled artisan that the inventor had possession of the claimed subject matter at the time of filing, is affirmed. See Purdue Pharma L.P. v. Faulding Pharmaceutical Co., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1487 (Fed. Cir. 2000).

2. Rejection under 35 U.S.C. § 102(b)

Claims 1-4, 6-11 and 13-20 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Cummins. Due to its brevity, the entire rejection is set forth below.

> See col. 4, lines 19-36, col. 5, lines 50-55, col. 6, lines 12-26, col. 13 [*sic*] [col. 12][1] and the claims. Such disclosure meets the claims.

Examiner's Answer, page 4.

We initially note that our review was significantly hampered by the examiner's statement of the rejection. The examiner merely cited sections of the Cummins reference, without correlating the teachings of that reference to the requirements of each individual claim. This leaves appellant and the merits panel to surmise the examiner's position. In reviewing the record, however, appellant appears to be sufficiently apprised as to the examiner's position, and we thus proceed to a decision on the merits.[2] See In re Kronig, 539 F.2d 1300,

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[1] The reference to column 13 in the rejection appears to be a typographical error. Appellant appears to recognize the error, as both the declaration and appellant's arguments are specifically directed to the example wherein a human multiple sclerosis patient was treated with alpha-interferon, which example appears at column 12 of Cummins.

[2] The fact that the issue is a rejection under section 102 of the statute allows us to proceed to the merits, because all the panel need determine is whether the reference discloses every limitation of the claimed invention, either explicitly or inherently. See In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1432 (Fed. Cir. 1997).

1302-3, 190 USPQ 425, 426-7(CCPA 1976). We thus affirm the rejection as it applies to claims 1-3, 6-11, 13-15 and 17-19.[3]

Appellant argues that Cummins is not prior art because it is not enabled, and contends that two declarations, submitted during prosecution, support that position. Cummins, appellant asserts, presents one anecdotal example describing treatment of multiple sclerosis, and presents no examples for the treatment of human lupus erythematosus. In fact, appellant asserts, most of the diseases described by Cummins have no autoimmune basis, but are of viral origin and/or are veterinarian diseases. Appellant argues that the instant specification, however, "has targeted a much broader spectrum of auto-immune diseases including 27 cases of multiple sclerosis and 18 cases of treating autoimmune conditions in animals." Appeal Brief, page 9.

The one anecdotal example wherein multiple sclerosis was treated, according to appellant, involved a patient who received treatment for twenty-one days, and had no recurrence of neurologic symptoms for nine months. Appellant argues that the result is not surprising because multiple sclerosis is a highly variable disease with "unpredictable periods of remission and relapse." Id. at 10. In addition, appellant asserts that the Cummins patent does not have claims drawn to multiple sclerosis or other autoimmune diseases, "most likely because the data failed to enable such claims." Id.

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[3] Claims 4, 16 and 20 are treated separately because Appellant states that the claims do not stand or fall together, see Appeal Brief, page 6, and separately

Appellant also argues that Cummins cannot anticipate the instantly claimed invention because of differences in the route of administration of the interferon. The instant claims require that the type one interferon be "ingested immediately upon administration." According to appellant, Cummins requires that the interferon be administered in such a manner so as to have maximum contact with the oral and pharyngeal mucosa. Appellant argues that the instant claims require, citing the 132 declarations of Dr. Lindsey and Dr. Wolinsky, contact with the gastric and intestinal mucosa. In the human studies, appellant asserts, citing the declaration of Dr. Lindsey, that even though there was brief contact with the oral mucosa, the contact was minimal, unlike the contact taught by Cummins, where increased contact is sought. See id. at 13-14. Thus, Appellant contends that Cummins teaches away from the immediate ingestion of interferon, as required by the instant claims. See id. at 11-12.

The burden is on the examiner to set forth a prima facie case of unpatentability. See In re Glaug, 283 F.3d 1335, 1338, 62 USPQ2d 1151, 1153 (Fed. Cir. 2002). In order for a prior art reference to serve as an anticipatory reference, it must disclose every limitation of the claimed invention, either explicitly or inherently. See In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1432 (Fed. Cir. 1997). During ex parte prosecution, however, claims are to be given their broadest reasonable interpretation consistent with

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argues the patentability of those claims, see id. at 14-15.

the description of the invention in the specification. See In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).

The Cummins reference states that human patients with conditions such as acute rheumatoid arthritis and multiple sclerosis were treated with human alpha-interferon at a dosage of 0.7 IU per pound twice a day. The interferon was retained in the mouth for one minute, and then either swallowed or discharged from the patient's mouth. See Cummins, Col. 12, lines 14-29.

With respect to the treatment of rheumatoid arthritis, an auto-immune disease, Cummins teaches that:

> Two patients suffering from rheumatoid arthritis were treated—a Caucasian male age 44 and a Caucasian female age 44. The male patient was pain free in 7 days, and the female was pain free in 10 days. They were both continued on the oral interferon for 21 days total and have remained asymptomatic.

Col. 12, lines 30-35

With respect to the treatment of a patient with multiple sclerosis, Cummins states:

> A 30-year-old Caucasian female nurse afflicted with multiple sclerosis and who had an extensive neurologic workup at City of Hope Hospital in Los Angeles received treatment in accordance with the present invention for 21 days. The patient has had no recurrence of her neurologic symptoms for the past nine months.

Col. 12, lines 40-45.

Thus, Cummins teaches all of the limitations of the claims. Cummins teaches a method of treating an auto-immune disease, such as rheumatoid arthritis or multiple sclerosis, through the administration of a type one interferon. Appellant's argument that the Cummins reference does not enable the present

claims because it presents a single anecdotal example is not found to be convincing. We recognize that in order for a reference to be anticipatory, it must be enabling. See In re LeGrice, 301 F.2d 929, 936, 133 USPQ 365, 372 (CCPA 1962) ("[B]efore any publication can amount to a statutory bar to the grant of a patent, its disclosure must be such that a skilled artisan could take its teachings in combination with his own knowledge of the particular art and be in possession of the invention."), In re Donohue, 766 F.2d 531,533, 225 USPQ 619, 621 (Fed. Cir. 1985) (reaffirming LaGrice). However, Cummins clearly states that the symptoms of patients with rheumatoid arthritis and multiple sclerosis were reduced upon treatment of oral interferon. In addition, although appellant's specification may disclose auto-immune diseases not discussed or taught by Cummins, the disclosure of a species anticipates the genus. Cummins teaches the treatment of rheumatoid arthritis and multiple sclerosis, both auto-immune diseases. In addition, although appellant asserts that because Cummins does not claim the treatment of an auto-immune disease the examiner must have deemed such claims not to be enabled by the specification, appellant presents no evidence to that effect. Finally, just because appellant provides data that was not presented by Cummins does not render the Cummins reference nonenabling.

The declarations of John William Lindsey and Jerry S. Wolinski have been considered, but are also not deemed to be convincing. Both declarations address whether the claims at issue in this appeal would have been obvious over the Cummins reference. The issue is not one of obviousness, however, but anticipation. In addition, with respect to the comments that one would have not have had a reasonable expectation of success of practicing the claimed method, Cummins teaches at the very least that the treatment of rheumatoid arthritis

patients and a multiple sclerosis patient resulted in the reduction of symptoms, and thus does teach that the method produced the desired result—the treatment of an auto-immune disease.

Appellant's arguments and the statements in the declarations that Cummins cannot anticipate the method claims at issue because of the purported differences in the route of administration of the interferon have also been considered, but are also not deemed to be convincing. The declarations state that the method of Cummins stresses that contact with the oral and pharyngeal mucosa should be maximized, whereas the instant claims require that the interferon be "immediately ingested upon oral administration." As noted above, during examination, the claims are to be given their broadest reasonable interpretation. The specification provides no special meaning for the word "ingest." Ingest, however, may be defined as "[t]o take or absorb (food) into the body." The American Heritage College Dictionary, Fourth Ed. Houghton Mifflin Co. (2002). The definition of ingest, and the use of the phrase "such that the type one interferon is ingested immediately upon oral administration" does not exclude adsorption of the interferon through the oral and/or pharyngeal mucosa as taught by Cummins. Thus, the claims are not limited to a method of delivery wherein contact with the oral or pharyngeal mucosa is avoided.

Appellant also argues that dosages used by Cummins are smaller than the dosages required by the instant invention. Cummins, according to Appellant, administered dosages ranging from 0.01 to 5 I.U. per day, whereas the instant application uses dosages ranging from 5 I.U./kg to about 50,000 I.U./kg.

That argument is not found to be convincing with respect to those claims wherein no dosage is recited, i.e., claims 1-3, 6-10, 13-15, 18, and 19. With respect to claim 11, wherein a dosage of "from about 5 I.U./kg to 50,000 I.U./kg"

is recited, that dosage corresponds to a dosage of 2.3 I.U./lb to 23,000 I.U./lb, see Appeal Brief, page 14, thus two dosages of 7 I.U./lb falls within the range recited, and the rejection is affirmed. The rejection with respect to claims 4, 16 and 20 is reversed, however, as the lower end of the range, i.e., 50 I.U./kg (Claims 4 and 16) and 166 I.U./ kg (Claim 20), is higher than the dosage used by Cummins.

3. Rejection under 35 U.S.C. § 103(a) over Cummins

With respect to the rejection of claims 5 and 12 as being rendered obvious by Cummins, the examiner states:

> The disclosure is the same as above as discussed for claims 1 and 8. The patent does not disclose an alternate day dosing. However, it does show that a daily dosage is possible, as a single dose or as divided and administered in a multiple daily dose regimen. The reference also teaches a staggered regimen of 1-3 days per week or month as an alternative to daily dosing. See col. 5, lines 50-55. With such a flexibility as taught by the reference, and since it is common knowledge in the art to employ such a regimen instead of continuous dosing, for a variety of reasons such as, toxicity, the condition of the patient, patient reaction and amelioration of the disease condition, etc., it would have been obvious to one of ordinary skill in the art to adopt an alternate day dosing and administer [interferon] as shown by Cummins for [multiple sclerosis].

Examiner's Answer, pages 4-5.

The portion of the Cummins patent relied upon by the examiner states that:

> Daily dosage of interferon can be administered as a single dose or, preferably, it is administered in a multiple-dose daily regimen. A staggered regimen, for example one to three days of treatment per week or month, can be used as an alternative to continuous daily treatment.

Col. 5, lines 51-56.

Appellant argues that the first portion of the above passage teaches a multiple-dose regimen rather than an alternate day regimen. In addition, according to appellant, although Cummins discloses a regimen of one to three days per week or month, that dosing regimen is also "alluded" by Cummins a being a less preferred mode of administration. The specific spacing of treatments is not discussed by Cummins, and thus, appellant contends that it is unclear whether this section refers to three continuous days of treatment, followed by a period without treatment, or single days of treatment separated by days without treatment. See Appeal Brief, pages 15-17. Thus, appellant concludes that the section relied upon by the examiner is non-enabling, as "[u]ndue experimentation would be necessary to try the other possible combinations days on therapy versus days off therapy." Id. at 17.

Appellant's arguments are not deemed to be convincing. Cummins teaches a variety of different treatment regimens, from daily to monthly. From those teachings, the ordinary artisan would have concluded that the spacing of the interferon treatments is not crucial to the success of the treatment method. "All the disclosures in a reference must be evaluated, including nonpreferred embodiments, ... and a reference is not limited to the disclosure of specific working examples." In re Mills, 470 F.2d 649, 651, 176 USPQ 196, 199 (CCPA 1972) (citations omitted). As the examiner notes, and appellant does not refute, it is common in the art to use alternate day dosing, and it is irrelevant that such alternate dosing schedules may have been less preferred mode of administration.

In addition, merely because Cummins does not explicitly disclose alternate day dosing does not lead to the conclusion that the reference is not enabled for such dosing. As noted above, alternate day dosing is commonly

used in the art, and given the variety of dosing schedules taught by Cummins, the ordinary artisan would have had a reasonable expectation of success that such an alternate day dosing could be used in the treatment method taught by Cummins.

4. Rejection under 35 U.S.C. § 103(a) over Cummins and Shibanti

Claims 1-20 stand rejected under 35 U.S.C. § 103(a) as being rendered obvious by the combination of Cummins and Shibutani. The entire rejection is set forth in its entirety below.

> The disclosure for the patent is as discussed above. The whole range of dosages claimed by the instant invention is not shown. However, the Shibutani abstract indicates that IFN toxicity studies with rats showed that it was tolerated well. Therefore, it would have been obvious to one of ordinary skill in the art to administer dosages higher than that shown in the patent with the reasonable expectation that such doses would not produce toxicity side-effects in humans. It would also have been obvious to employ such an alternate day dose regimen instead of continuous dosing, for a variety of reasons such as, toxicity, the condition of the patient, patient reaction and amelioration of the disease condition, etc.

Examiner's Answer, page 5.

Again, the panel would like note that the examiner has entered a shotgun rejection of all of the claims, rather than performing a claim-by-claim analysis. The only claims that require a specific range of dosages are 4, 11, 16, and 20, and the rejection is only analyzed as it applies to those claims.

Appellant argues that the declarations filed under 37 CFR § 1.132 discuss the issue of dosage. According to appellant, the dosages found to be the most effective in the instant application do not overlap the dosages taught by

Cummins, and in fact, are two orders of magnitude greater than those used by Cummins.

The burden is on the examiner to set forth a prima facie case of obviousness. See In re Alton, 76 F.3d 1168, 1175, 37 USPQ2d 1578, 1581 (Fed. Cir. 1996). In assessing the prior art, each prior art reference must be considered in its entirety in an obviousness determination. In re Wesslau, 353 F.2d 238, 241, 147 USPQ 391, 393 (CCPA 1965). In assessing the teachings of the prior art reference as a whole, the examiner must also consider those disclosures that may teach away from the invention. See In re Fine, 837 F.3d 1071, 1074, 5 USPQ2d 1596, 1598 (1988).

In this case, Cummins teaches that the amount of interferon should be used in amounts of "less than 5 IU/lb of body weight," Col. 3, lines 9-12, and characterizes the method as "using interferon in low oral dosages," Col. 1, lines 6-14. Thus, Cummins teaches away from using higher dosages, and thus there is no motivation for increasing the dosage amount of interferon. Thus, the examiner has not set forth a prima facie case of obviousness, and the rejection over the combination of Cummins and Shibutani is reversed.

CONCLUSION

The rejections under 35 U.S.C. § 112, first paragraph, 35 U.S.C. § 102(b) as it pertains to claims 1-3, 6-11, 13-15, and 17-19, and 35 U.S.C. § 103(a) over

Cummins of claims 5 and 12 are affirmed. The rejections under 35 U.S.C. § 102(b) as it pertains to claims 4, 16, and 20, and 35 U.S.C. § 103(a) of claims 1-20 over the combination of Cummins and Shibutani, however, are reversed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART; REVERSED-IN-PART

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)
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